GUIDELINES FOR THE MANAGEMENT OF MOTOR NEURONE DISEASE (MND)

PREPARED BY

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AND ENDORSED BY COUNCIL OF THE ASSOCIATION OF BRITISH NEUROLOGISTS

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Guidelines for the Management of Motor Neurone Disease

These evidence based guidelines for the management of motor neurone disease (MND) have been developed by the [+]Excerpta Medica MND Advisory Group in consultation with the University of Birmingham Clinical Trials Unit. Suggestions received following review of an earlier draft by Council and the Services Committee of the ABN were incorporated into a subsequent draft which was presented at a meeting open to the general membership of the ABN at its Southampton meeting in March 1999. Further comments, received from the ABN membership, are incorporated in this document.

Current status of diagnosis

The World Federation of Neurology (WFN) Research Group on Neuromuscular Diseases has recently updated the El Escorial Criteria for the Diagnosis of MND [1] [http://www.wfnals.org/Airlie criteria/]. Although widely accepted these criteria were designed as an aid to clinical trials and research. They are thus more restrictive than those used in routine neurological practice and have not been validated in a population based setting.

Telling the diagnosis

- The diagnosis should be communicated by a senior doctor, in privacy, with the opportunity for an early follow-up appointment.
- Patients should be accompanied by a relative and/or health professional who would be able to provide immediate support.
- Regular feedback is essential, to ensure patients have understood the information that they have been given [2] and they should be encouraged to express their concerns.
- Written information should be available about the disease, the Motor Neurone Disease Association and other follow-up contacts.
- The diagnosis should be communicated to the General Practitioner without delay.

Principles of General Management

A co-ordinated multidisciplinary approach is required to meet the rapidly changing physical and psychosocial needs of patients and carers throughout the course of the disease. This should be underpinned by the following principles:

- Care encompassing the whole person and those that matter to them
- Quality of life and prompt provision of treatments to secure symptom control
- Respect for patient autonomy and choice
- Emphasis on open and sensitive communication
- Planning for the future and timely liaison with the palliative care team.

Symptom Management

The maintenance of optimal functional independence and well-being requires a multidisciplinary approach.

- **Drooling** can be alleviated by anti-cholinergic drugs such as hyoscine (sublingual or transdermal), glycopyrrolate (subcutaneously), atropine (orally), tricyclic antidepressants (such as amitriptyline) and beta-blockers [3]. Non-pharmacological approaches such as salivary gland irradiation and duct ligation have been described.
- **Dysphagia** is best managed in association with speech and language therapists as well as dietitians, and as it progresses more invasive approaches such as PEG need to be considered, in consultation with patient and carer. Expert opinion favours early PEG, but more evidence is required.

- Speech and language therapists provide important advice on the management of **communication** difficulties. When a communication aid is needed it is essential that it is provided promptly.
- **Muscle cramps** may be treated by quinine, diazepam, phenytoin and naftidrofuryl.
- **Spasticity** can be helped by physiotherapy or drug treatment e.g. baclofen, dantrolene, tizanidine.
- The impact of increasing limb **weakness** may be alleviated by specific interventions ranging from low-tech equipment such as simple splints and the neck support collars designed for MND sufferers to environmental control systems (POSSUM)
- **Respiratory** symptoms are distressing for patients and carers. Nocturnal hypoventilation may cause early morning headache and lethargy. Non-invasive respiratory support should be considered at an early stage with appropriate specialist respiratory advice in discussion with patients and carers. Other symptomatic treatments such as opioids can relieve dyspnoea, coughing and choking. The *Breathing Space Kit contains medication which can be used by the carer, nurse or general practitioner for the emergency treatment of the acute episodes of respiratory distress which often occur in the terminal stages. The use of invasive ventilation is a complex issue which requires early, careful discussion with patients and carers
- **Depression** should be differentiated from the natural sadness of disability, but when genuinely present can be treated with an appropriate antidepressant, such as amitriptyline and SSRIs. These drugs may also relieve **emotional lability** and **anxiety**. Psychiatric guidance may also be required.
- **Pain** is commonly experienced, and may be managed at any stage with anti-spasticity drugs, non-steroidal agents, and analgesics, using the principles of the WHO Ladder including opioids such as oral morphine or transdermal fentanyl patches. Significant benefits can be achieved with physiotherapy and occupational therapy interventions.

Disease modifying therapy in MND

Reviews of some of these therapies are currently registered with the Cochrane Collaboration [http://www.cochrane.co.uk]. It is hoped that the coverage of this area will become more comprehensive in the future. These guidelines are based on clinical effectiveness only and do not consider the issue of cost. The latter is a matter for others to consider e.g. the National Institute for Clinical Excellence.

- **Riluzole** is the only drug currently licensed in the UK for the treatment of MND. Riluzole is a disease modifying therapy. It does not cause symptomatic improvement and does not prevent death. Patients and carers need to be informed of the implications of the trial data before starting treatment. Evidence for its efficacy comes from two randomised placebo controlled trials (RCTs) [4,5], see footnote[o]. The possibility of riluzole treatment is appropriately discussed with MND patients as soon as a working diagnosis has been made, although RCT evidence only currently exists for patients with definite or probable MND by the El Escorial Criteria [1]. Patient choice or adverse effects, such as fatigue and nausea, may lead to cessation of therapy. Efficacy evidence from placebo-controlled randomised clinical trials only extends to 18 months therapy. Nonetheless it is reasonable to continue therapy for longer than 18 months if considered appropriate by the clinician, patient and carers. However, it is inappropriate to start patients with advanced disease on riluzole or to prolong treatment into the terminal phase.
- Although there is published evidence from one placebo-controlled RCT [8] that **insulin-like nerve growth factor (rhIGF-1)** slows disease progression, this was not confirmed in a second RCT [9]. This drug is not licensed.
- Many **other putative disease modifying therapies** for MND have been investigated but have not been shown to be effective in RCTs.

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* Obtainable on medical prescription through the Motor Neurone Disease Association, David Niven House, PO Box 246, NORTHAMPTON, NN1 2PR. (Telephone 01604-250505, fax 01604-24726). Kit includes suggestions for the management of acute respiratory symptoms and a selection of 2ml and 5ml syringes with appropriate needles. It is stocked with drugs through prescription by the GP. The following contents are suggested:

Diazepam	enema (Stesolid) 10mg x 3	(for use by carer)
Diamorphine	for injection 5mg x 3	(for use by nurse or doctor)
Chlorpromazine	for injection 25mg x 3	(for use by nurse or doctor)
Hyoscine	for injection 0.4mg x 3	(for use by nurse or doctor)
Water	for injection 5mls x 3	(for use by nurse or doctor)

Midazolam 5mg -10mg x 3 for injection is suggested as a possible alternative to chlorpromazine

[o] These RCT's report a modest decrease in risk of tracheostomy or death with riluzole (relative risk riluzole 100mg/day = 0.66 (95% confidence interval 0.42-1.02.), p = 0.05 over 12 months treatment, [4]; relative risk, riluzole 100mg/day (Cox model) = 0.65 (95% confidence interval 0.50-0.85), p = 0.002 over 18 months treatment, [5]. It has been calculated [6] that the number of patients needed to treat with riluzole 100mg/day to prevent one death or tracheostomy after one year (based on [5]) is 9.2 (95% confidence interval 5.2-38). A post-hoc analysis of the data from the dose ranging trial [7] has suggested that riluzole delays the progression of the disease to severe disability. The findings of this preliminary study require confirmation.

References

1. World Federation of Neurology Research Group on Neuromuscular Diseases. El Escorial World Federation of Neurology criteria for the diagnosis of amyotrophic lateral sclerosis. J Neurol Sci 1994; 124 (Suppl): 96-107].
2. Johnston M, Earll L, Mitchell E, Morrison V, Wright S. Communicating the diagnosis of motor neurone disease. Palliative Medicine 1996; 10: 23-34.
3. Newall AR, Orser R, Hunt M. The control of oral secretions in bulbar ALS/MND. J Neurol Sci 139: Suppl:43-4. 1996.
4. Bensimon G, Lacomblez L, Meininger V et al. A controlled trial of riluzole in amyotrophic lateral sclerosis. N Eng J Med 1994; 330: 585-91
5. Lacomblez L, Bensimon G, Leigh PN et al. Dose ranging study of riluzole in amyotrophic lateral sclerosis. Lancet 1996; 347: 1425-31
6. Anon. Riluzole. In Therapeutic Drugs, ed. Dollery C. Churchill Livingstone, Edinburgh 1999; R37-41
7. Riviere M, Meininger V, Zeisser P, Munsat T. An analysis of extended survival in patients with amyotrophic lateral sclerosis treated with riluzole. Arch Neurol 1998; 55: 526-8
8. Lai EC, Felice KJ, Festoff BW et al. Effect of recombinant human insulin-like growth factor-1 on progression of ALS. Neurology 1997; 49: 1621-30
9. Borasio G, Robberecht W, Leigh PN et al. A placebo-controlled trial of insulin-like growth factor-1 in amyotrophic lateral sclerosis. Neurology 1998; 51: 583-6

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